PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference DIAKR.007VPC	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US 03/28527	International filing date *(day/month/year)* 11.09.2003	Priority date *(day/month/year)* 12.09.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/4422		
Applicant DIAKRON PHARMACEUTICALS, INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03.04.2004	13.12.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Economou, D Telephone No. +49 89 2399-8599

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US 03/28527

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-71 as originally filed

Claims, Numbers

1-11 as originally filed

Drawings, Sheets

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-4 (all partially),5,6,7-8 (all partially),9-11

   because:

   ☒ the said international application, or the said claims Nos. 3,5,8 with regard to IA (see separate sheet, item 1a) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 3,5 (see separate sheet, item 2) are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 1-4 (all partially),6,7-8 (all partially), 9-11

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-4 (all partially), 5,7-8 (all partially) .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	8 (see separate sheet, item 3)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	8 (see separate sheet, item 3)
Industrial applicability (IA)	Yes:	Claims	3,5,8 (see separate sheet, item 1)
	No:	Claims	

2. Citations and explanations

see separate sheet

1). a). Claims 3,5 and 8 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

b). For the assessment of the present claims 3,5 and 8 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

2). The inhibition of calcium T-channel activity in itself (see claim 1) is not a therapeutic application since this effect still needs to find a practical application in the form of a defined, real treatment of any pathological condition in order to make a technical contribution to the art and to be considered as an invention. Hence, the subject-matter of claims 3 and 5 (due to its dependence to claim 1) which appears to relate to a method of therapy, is not clear since it does not define the pathological condition treated by the administration of the T-channel antagonist (see in contrast claim 8).

3). The subject-matter of claim 8 is novel since it is not disclosed thus far in the available prior art.
The subject-matter of claim 8 does not involve an inventive step since the skilled person knows from **D1** (=KUMAR P P ET AL: "Synthesis and evaluation of a new class of Nifedipine analogs with T-type calcium channel blocking activity" MOLECULAR PHARMACOLOGY, BALTIMORE, MD, US, vol. 61, no. 3, March 2002 (2002-03), pages 649-658, XP002237191 ISSN: 0026-895X) that the compounds of formula (I) are T-type calcium channel blockers. The fact that T-type channel blockers are used for the treatment of essential hypertension in dosages spaced at least one day apart is known form **D2** (=KOBRIN, I. ET AL.: "Safety of Mibefradil, a New Once-a-Day, Selective T-Type Calcium Channel Antagonist" AMERICAN JOURNAL OF CARDIOLOGY, vol. 80, no. 4B, 1997, pages 40c-46c, XP002267729) for the T-type channel blocker mibefradil. Hence, the subject-matter of claim 8 is obvious by combining the teachings of **D1** with **D2**.

4). In case the present application would enter the European Phase, WO 03/062201 (Publ. date: 31.07.2003; Prio. dates: 18.01.2002 and 11.03.2002; Filing date: 14.01.2003) would be prejudicial to the novelty of the present application since it discloses compounds of formula (I) for the treatment of hypertension (see page 48, paragraph [0107]).